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Original Article

Stereoselective Photodimerization of 2-Anthracenecarboxylic Acid Using a Cation-Charged γ-Cyclodextrin Template*

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Abstract

Two pyridinium groups were introduced into γ-cyclodextrin (γ-CD) at the A and E glucose units to make a molecular flask for controlling the *stereo*-selectivity of photodimerization of 2-anthracenecarboxylic acid. When the photodimerization of 2-anthracenecarboxylic acid was carried out in the presence of bispyridinio-appended γ-CD, the relative yield of one of the configurational isomers was increased 1.5-fold compared to the corresponding yield in aqueous solution. The optical yields of the photodimerization reaction products also increased more than 10-fold by the addition of bispyridinio-appended γ-CD.

Introduction

γ-Cyclodextrin is a cyclic compound composed of eight D-glucose residues joined by α-1,4-linkages, which together form a large central cavity that can accommodate two other molecular species. Because of this unique property, γ-cyclodextrin can be used as a molecular flask or vessel, in which interactions or reactions between two guest molecules are facilitated [1–4]. *Regio*- and *stereo*-selective reaction between two substrates can be mediated in the γ-CD cavity.

Two 2-anthracenecarboxylic acids undergo photodimerization to produce four kinds of configurational isomers (Scheme 1). The relative yield of each configurational isomer is dependent on the degree of steric hindrance and electrostatic repulsion between two carboxylate units. γ-Cyclodextrin is able to accommodate two molecules of 2-anthracenecarboxylic acids and can be used as the molecular flask for the photodimerization reaction [5–7]. When the photodimerization of 2-anthracenecarboxylic acid is carried out in the presence of γ-CD, photodimerization is accelerated and the relative yields of the configurational isomers changes according to the stability of the inclusion complex. If γ-cyclodextrin is modified at the two particular glucose units with two cation-charged moieties, its binding ability for 2-anthracenecarboxylic acids increases due to electrostatic interactions. Furthermore the orientation of the two 2-anthracenecarboxylic acid molecules within the γ-CD cavity can be regulated. We reasoned that a simple pyridinio-modified γ-CD might allow us to regulate the photodimerization of 2-anthracenecarboxylic acid. We used a bispyridinio-modified γ-cyclodextrin (**Py2-CD**), in which the two particular glucose units are derivatized with two pyridinium cations, to increase the *regio*- and *stereo*-selectivity of the photodimerization of 2-anthracenecarboxylic acid. In this paper, we report a remarkable template effect of bispyridinio-modified γ-CD for the photodimerization of 2-anthracenecarboxylic acid.

Experimental

General

Mass spectra were obtained on a Shimadzu MALDI III (TOF-MS). ^{1}H-NMR spectra were recorded on a Varian VXR-500S FT-NMR spectrometer. D_2O ($\delta = 4.7$) was used as an internal standard, and tetramethylsilane (TMS, $\delta = 0$) was used as an external standard. HPLC analyses were performed with a Shimadzu LC-VP system equipped with Nakarai COSMOSIL 5C18-AR2 and Daisel Chiralcel OJ-RH. β-Cyclodextrin was a kind gift from Nihon Shokuhin Kako Ltd. Other reagents were purchased from Tokyo Kasei. D_2O with an isotopic purity of 99.95%, was purchased from Merck.

Material

Synthesis of ***Py2(AE)-γ-CD***

6A,6E-bistosyl-γ-CD (100 mg) was heated in pyridine (20 mL) at 80 °C for 12 h to obtain 6A,6E-bispyridinio-

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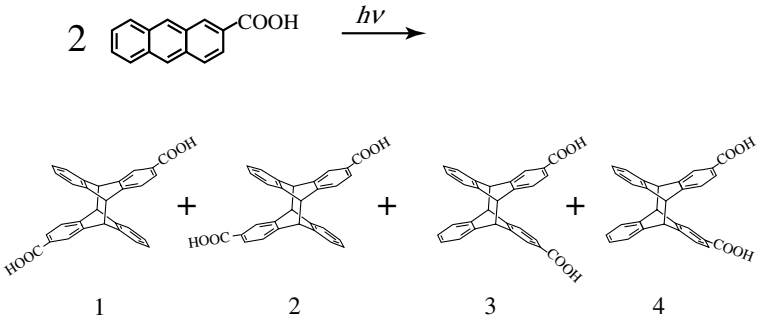


Scheme 1. Photodimerization of 2-anthracenecarboxylic acid.

γ-CD (**Py2(AE)-γ-CD**). The reaction mixture was concentrated under reduced pressure. The crude product was dissolved in water followed by column chromatography with QAE Sephadex A-25 to change counter anions of **Py2(AE)-γ-CD** from TsO^- to Cl^-. The lyophilization of the fraction solution containing the desired product gave a white powder (67.2 mg, yield 72.4%).

MALDI-TOFMS: *m/z*: calcd for $C_{58}H_{88}O_{38}N_2$: 1420.5; found: 1420.8 $[M]^+$. ^1H NMR (500 MHz, D_2O): δ =2.73 (dd, $J = 4.4$, 12.5 Hz, 2H, H-6B, H-6F), 2.97 (dd, $J = 1.5$, 12.5 Hz, 2H, H-6B', H-6F'), 4.99 (d, $J = 3.9$ Hz, 2H, H-1), 5.03 (d, $J = 3.7$ Hz, 2H, H-1), 5.06 (d, $J = 3.9$ Hz, 2H, H-1), 5.16 (d, $J = 3.8$ Hz, 2H, H-1), 8.10 (t, $J = 6.8$ Hz, 4H, Py-3), 8.62 (t, $J = 6.8$ Hz, 2H, Py-4), 8.87 (d, $J = 6.8$ Hz, 4H, Py-2).

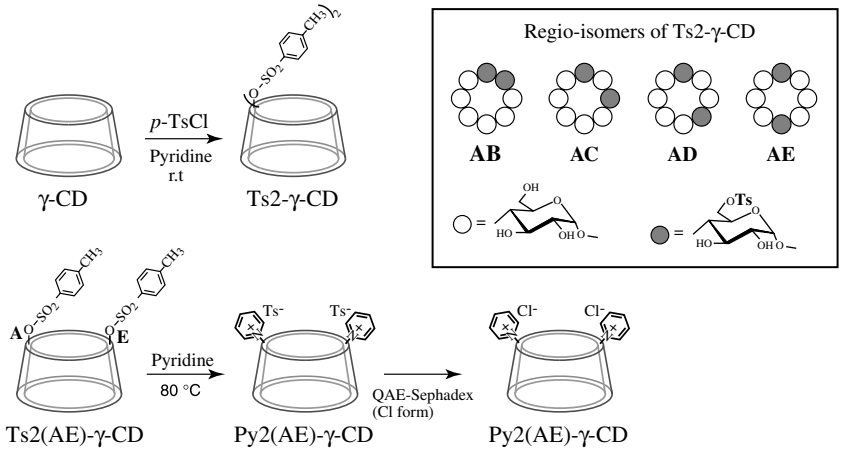
Methods

A solution of 2-anthracenecarboxylic acid (0.1 mM, 1.0 mL) in pH 9.1 carbonate buffer (20 mM, 5% ethylene glycol) was applied to a quartz cell and degassed with nitrogen for 10 min. The solution was photoirradiated with Hamamatsu PHOTOCURE 200 (200 W Hg–Xe, $\lambda > 370$ nm) equipped with an optical glass filter (Toshiba UV-35) under nitrogen bubbling. At regular intervals, a small aliquot of the solution was sampled, suitably diluted, and assayed by HPLC.

Results and discussion

γ-Cyclodextrin was modified with two pyridinium groups at the A and E glucose units (Scheme 2). 6A,6E-bistosyl-γ-CD [8] was heated in pyridine at 80 °C for 12 h to obtain 6A,6E-bispyridinio-γ-CD (**Py2(AE)-γ-CD**) [9–11]. Counter anions of **Py2(AE)-γ-CD** were changed from TsO^- to Cl^- by ion exchange chromatography. Monopyridinio-modified γ-CD (**Py-γ-CD**) was also prepared by a similar method to that of **Py2(AE)-γ-CD**.

The binding constant of **Py2(AE)-γ-CD** for 2-anthracenecarboxylic acid was estimated from the dependence of the absorption intensity of 2-anthracenecarboxylic acid at 386 nm on the concentration of **Py2(AE)-γ-CD** using the curve-fitting to the 1:2-host/guest-type Benesi–Hildebrand equation [12]. The binding constant of **Py2(AE)-γ-CD** for 2-anthracenecarboxylic acid is 9.4×10^7 M^{-2}, which is 12-fold greater than that of unmodified γ-cyclodextrin (Table 1). The binding constant of mono-pyridinio-modified γ-CD (**Py-γ-CD**) for 2-anthracenecarboxylic acid is only 1.8-fold greater than that of unmodified γ-cyclodextrin. This result suggests that both the carboxylate anions of the two 2-anthracenecarboxylic acid molecules interact with the pyridinium cations of **Py2(AE)-γ-CD** and that this two ion interaction cooperatively stabilizes the 1:2 inclusion complex of **Py2(AE)-γ-CD**.



Scheme 2. Synthesis of 6A,6E-bispyridinio-γ-CD (Py2(AE)-γ-CD).

Table 1. Binding constants of γ-CD and cation-charged γ-CDs for 2-anthracenecarboxytlic acid

Host	$K_b/10^7$ M^{-2}
γ-CD	0.8
Py-γ-CD	1.4
Py2(AE)-γ-CD	9.4

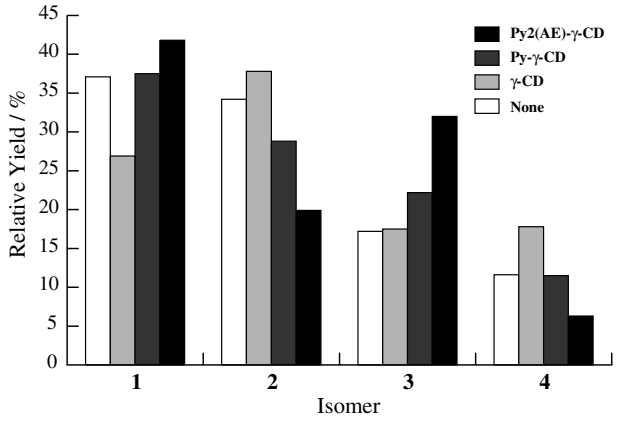


Figure 1. Effect of ion–interactions on the *regio*-selectivity for the photodimerization of 2-anthracenecarboxylic acid.

The photodimerization reaction of 2-anthracenecarboxylic acid was carried out in the presence of either **Py2(AE)-γ-CD**, **Py-γ-CD**, or unmodified γ-CD. As a control, the reaction was also performed in the absence of any γ-CD. The relative yield of the isomer **3** increased 1.5-fold in the presence of **Py2(AE)-γ-CD** compared with the condition of its absence, whereas that of the isomer **2** fell by about a half. However the effect of **Py-γ-CD** to change the relative yields of the configurational isomers was small. These results suggest that the electrostatic interaction between the pyridinium cations and the carboxylate anions could moderately regulate the configurational selectivity of the photodimerization. Indeed there was a significant increase in yield of the isomer **3** by the addition of **Py2(AE)-γ-CD**. The product isomer distribution primarily depends on the population of these orientational isomers in the ground state before photodimerization. Because of the confined space for the substrate molecule within the CD cavity, its orientation is severely restricted. Exclusion and re-association of the substrate within the lifetime of the excited singlet state is not possible, and thus the product structure reflects that of the precursor ground state complex in the CD cavity. Our results indicate that the precursor complex of the isomer **3** is stabilized by the two pyridinio cations of **Py2(AE)-γ-CD**, although the precursor complex of the isomer **3** in aqueous solution or in the unmodified γ-CD cavity is less stable, probably because of electrostatic repulsion of carboxylate anions (Figure 1).

There are enantiomers in the case of the isomer **2** and **3**. The addition of **Py2(AE)-γ-CD** or **Py-γ-CD** induced

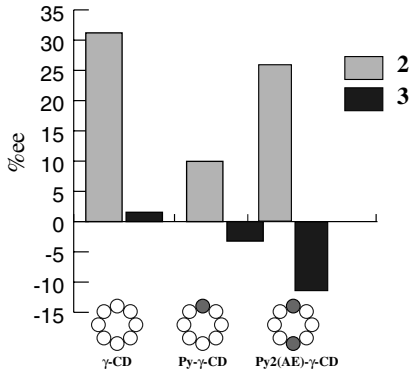


Figure 2. Effect of ion–interactions on the *enantio*-selectivity for the photodimerization of 2-anthracenecarboxylic acid.

enantio-differentiating photodimerization. **Py2(AE)-γ-CD** increased the ee 10-fold for the isomer **3**, compared with the reaction using unmodified γ-CD. The electrostatic interactions between the pyridinium cations and the carboxylate anions are highly effective in regulating the enantioselectivity and this result suggests that both of the two electrostatic interaction act for the enantioselectivity. These electrostatic interactions between the pyridinium cations and the carboxylate anions in the cavity of **Py2(AE)-γ-CD** favor one of the diastereomeric precursors of the isomer **3**, although the stabilities of two diastereomeric precursors of the isomer **3** are almost the same in the unmodified γ-CD cavity. Since there is only one electrostatic interaction with the diastereomeric precursors of the isomer **2** in the cavity of **Py2(AE)-γ-CD**, **Py2(AE)-γ-CD** cannot perturb the relative stability of the diastereomeric precursors of the isomer **2**, and the ee of the isomer **2** in the presence of **Py2(AE)-γ-CD** is almost same as that done in the presence of unmodified γ-CD (Figure 2).

Conclusion

Py2(AE)-γ-CD, which has two pyridinium units at the A and E glucose units, is an effective molecular flask to regulate the configurational selectivity and the enantioselectivity of the photodimerization of 2-anthracenecarboxylic acid. This regulation was due to electrostatic interactions between the pyridinium cations of the host molecule and the carboxylate anions of the guest molecules.

Acknowledgements

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